PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

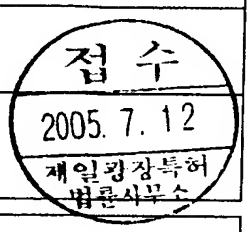
(PCT Rule 43bis.1)

Date of mailing *(day/month/year)*	**11 JULY 2005 (11.07.2005)**
Applicant's or agent's file reference PCA40850/HMY - KS	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/KR2005/000586	**03 MARCH 2005 (03.03.2005)**	12 MARCH 2004 (12.03.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC7 C07D 495/04



Applicant

HANMI PHARM. CO., LTD. et al

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.
For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/KR	Authorized officer
Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea	LEE, Jae Jeong
Facsimile No. 82-42-472-7140	Telephone No. 82-42-481-5604

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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material
   - ☐ a sequence listing
   - ☐ table(s) related to the sequence listing

   b. format of material
   - ☐ in wirtten format
   - ☐ in computer readable form

   c. time of filing/furnishing
   - ☐ contained in the international application as filed.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additioanl copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1 - 15	YES
	Claims		NO
Inventive step (IS)	Claims	1 - 15	YES
	Claims		NO
Industrial applicability (IA)	Claims	1 - 15	YES
	Claims		NO

2. Citations and explanations :

Reference is made to the following documents:

D1: WO 02059128 A2 (CADILA HEALTHCARE LTD.) 01 AUG. 2002
D2: WO 9851689 A1 (SANOFI) 19 NOV. 1998
D3: US 5204469 (SANOFI) 20 APR. 1993
D4: WO 0043397 A1 (NEUROSEARCH A/S) 27 JULY 2000
D5: WO 02094802 A1 (GRUNENTHAL GMBH) 28 NOV. 2002
D6: EP 555153 A1 (ROUSSEL-UCLAF) 05 FEB. 1993

The present invention relates to a method of preparing thieno[3,2-c]pyridine derivatives. Ticlopidine and clopidogrel having high blood platelet aggregation inhibitory and anti-thrombotic activities are prepared by reacting a substituted thiophene derivative with a 2-chlorobenzylamine derivative. Further, it relates to several compounds as an intermediate for the preparation of a thieno[3,2-c]pyridine derivatives.

D1 - D3 disclose various processes for the preparation of thieno[3,2-c]pyridine derivatives, such as clopidogrel. The compounds of the D1 - D3 are pharmacologically active and have significant anti-aggregating and anti-thrombotic properties.

D4 provides certain fused heterocyclic compounds and their use in treatment of neurodegenerative diseases and for the regeneration or prevention of degeneration of lesioned and damaged neurons.

D5 relates to substituted C-furan-2-yl-methylamine and C-thiophen-2-yl-methylamine derivatives, a method for the production thereof, medicaments and pharmaceutical compositions containing said derivatives.

D6 discloses new pyrethrinoid ester(s) derived from furfuryl or thiophenyl alcohol useful as insecticides, nematicides or acaricides.

Although D1-D3 teach the process for preparing thieno[3,2-c]pyridine derivatives, such as ticlopidine or clopidogrel, and D4-D6 teach the using various fused heterocyclic compounds, D1-D6 do not disclose the features of the subject matter of claims 1 - 15, which meet the criteria set forth in PCT Article 33(2), (3) and (4). The preparation method of thieno[3,2-c]pyridine derivatives and several compounds as an intermediate for the preparation of a thieno[3,2-c]pyridine derivatives in this invention are not anticipated by any of the references on record.

Thus, the invention described in the present application is considered to be novel, inventive and industrially applicable.